added.

Claims 1 and 5-9 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

II. Rejection of Claims 1 and 5-9 Under 35 U.S.C. § 101

The Action first rejects claims 1 and 5-9 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

As set forth in Applicants' response mailed on March 12, 2003 ("the previous response") to the First Office Action in this case, which was mailed on December 13, 2002 ("the First Action"), the present invention has a number of substantial and credible utilities, not the least of which is in diagnostic assays, as described in the specification, at least at page 10, lines 27-33. As described in the specification from page 15, line 33 through page 16, line 32, the present sequence defines several coding single nucleotide polymorphisms - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position 91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in an valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7. As such

polymorphisms, and particularly combinations of polymorphisms, are the basis for **forensic** analysis, which does not require any information at all about the ultimate biological function of the encoded protein, and is undoubtedly a "real world" utility, the present sequences must in themselves be useful.

The Examiner questions this asserted utility, stating "(s)uch assays can be performed with any polynucleotide" (Action at page 6). This argument is flawed in a **number** of respects. First, Applicants submit that the asserted forensic utility is specific precisely because it cannot be applied to just any polynucleotide. In fact, the basis for forensic analysis is the fact that such polymorphic markers are **not** present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Second, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. The Examiner appears to be attempting to use the information presented for the first time by Applicants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Applicants discovery is completely improper. Third, as set forth in the previous response, the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Importantly, the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. This case, and particularly the cited quote, **directly** rebuts the Examiner's argument, which is presumably why the Examiner failed to address the holding of *Carl Zeiss* in the Action. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the

Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Applicants respectfully point out that the presently described polymorphisms are useful in forensic analysis for the same reason that any marker is useful in forensic analysis - specifically, to specifically identify individual members of the human population based on the presence or absence of the described polymorphism. Using the polymorphic markers as described in the specification as originally field can distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis **clearly** is a real world, practical utility. As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such

evidence from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Furthermore, as the Examiner admits that the presently described polymorphism is a part of the family of polymorphisms that have a "well established" utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis exactly as they are described in the specification as originally filed, without the need for any further research. Even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain this polymorphic marker, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As

stated above, using the polymorphic markers as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin*, *supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as set forth in the previous response, the present sequence has a number of additional patentable utilities, among them, as detailed in the specification at least at page 2, line 36, the present nucleotide sequences have a specific utility in "identification of coding sequence". This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11 (present within the chromosome 11 clone presented in GenBank Accession Number AP003071; alignment and the first page from the GenBank report are presented in **Exhibit B**). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. The specification details, from page 10, line 33 to page 11, line 2, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Applicants respectfully submit that the

practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

As yet a further example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 3, line 2, the present nucleotide sequences have a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11, as detailed above (**Exhibit B**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, the Examiner is invited to review, for example, section 3 of Venter *et al.* (2001, Science *291*:1304, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions these asserted utilities, stating once again that "(s)uch assays can be

performed with any polynucleotide" (Action at page 7). This argument is also flawed in a number of respects. First, Applicants point out that only a small number of other nucleotide sequences can be used to map the protein coding regions in this specific region of chromosome 10. Thus, this analysis can **not** "be performed with any polynucleotide". Second, the Examiner once again seems to be confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 10 does not mean that the use of Applicants' sequence to map the protein coding regions of chromosome 10 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

In the previous response, Applicants detailed an additional example of the utility of the present nucleotide sequences, as described in the specification at page 5, lines 35-37, specifically that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Applicants point out that nucleic acid sequences are commonly used in gene chip applications without **any** information regarding the function of the encoded protein, or even evidence regarding whether the sequence is actually even expressed. Thus, the present sequence, which has been biologically validated to be expressed, has a much greater utility than sequences that are merely predicted to be expressed based on bioinformatic analysis. Additionally, Applicants point out that nucleic acid sequences such as SEQ ID NO:6 are routinely used by companies throughout the biotechnology sector **exactly** as they are presented in the Sequence Listing, without **any** further experimentation. Expression profiling does **not** require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types.

As previously set forth, evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments from genes in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. Affymetrix is clearly a "real world" company, as evidenced the fact that the United States Patent and Trademark Office has issued numerous U.S. Patents to Affymetrix covering gene chip technology, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip

formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). Given the widespread utility of such "gene chip" methods using non-biologically validated, *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* biologically validated coding sequence would have great utility in such DNA chip applications. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Furthermore, compositions that enhance the utility of such DNA chips must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions this utility, stating that "all nucleic acids and genes are in some combination useful in polynucleotide arrays" (Action at page 7). However, the Examiner once again seems to be confusing the requirements of a **specific** utility with a **unique** utility. Simply because other polynucleotide sequences can be used to track gene expression on a gene chip does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Additionally, in the previous response, Applicants pointed out that a sequence sharing nearly 100% percent identity at the protein level over extended portions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "Homo sapiens two-pore calcium channel protein 2" (GenBank accession number AY029200; alignment and GenBank report shown in **Exhibit C**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is an ion channel protein.

The Examiner questions this asserted utility, again citing articles by Doerks *et al.* (Trends in Genetics *14*:248-250, 1998; "Doerks"), Brenner (TIG *15*:132-133, 1999; "Brenner"), and Bork *et al.* (Trends in Genetics *12*:425-427, 1996; "Bork") to support the argument that "the assignment of function based on homology is inherently difficult" (Action at page 6). Applicants addressed the

shortcomings of each of these references in the previous response, but the Action does not comment on Applicants' arguments at all. Therefore, Applicants will again address the shortcomings of each of these references, and then address the argument of whether such articles support an alleged lack of patentable utility.

The Action cites Doerks for the proposition that sequence-to-function methods of assigning protein function are prone to errors. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional information becomes available for at least one member" (Doerks, page 248, paragraph bridging columns 1 and 2, emphasis added). Applicants point out that, as detailed above, a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as a two-pore calcium channel protein (see **Exhibit C**). The two-pore ion channel superfamily is a well-studied protein family with a large amount of known functional information, exactly the situation that Doerks suggests will "simplify" and "avoid the pitfalls" of previous sequence-to-function methods of assigning protein function (Doerks, page 248, columns 1 and 2). Thus, instead of supporting the Examiner's position against utility, Doerks actually supports Applicants' position that the presently claimed sequences have a substantial and credible utility.

The Examiner cites Brenner as teaching that "most homologs must have different molecular and cellular functions" (the First Action at page 5). However, this statement is based on the assumption that "if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions" (Brenner, page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is "an issue solvable by appropriate use of modern and accurate sequence comparison procedures" (Brenner, page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the "modern and accurate sequence comparison procedures" used by Applicants. Thus, the Brenner article also does not support the alleged lack of utility.

The Examiner finally cites Bork as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable, based on the "structural similarity of a small

domain of the new protein to a small domain of a known protein" (the First Action at page 5). Thus, the Examiner's reliance on Bork has the same failing as described above for Doerks, specifically, the assumption that Applicants assertion that the present sequence is an ion channel protein is made on the basis of structural similarity of a small domain of the new protein to a small domain of a known protein. Applicants again would like to invite the Examiner's attention to the fact a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as a two-pore calcium channel protein (see **Exhibit C**). Thus, Applicants assertion that the present sequence is an ion channel protein is not made on the basis of "structural similarity of a small domain of the new protein to a small domain of a known protein", but rather vast homology over large tracts of the sequence. Thus, Bork also does not support the alleged lack of utility for the present invention.

Thus, while Applicants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a calcium channel protein, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode a calcium channel protein. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Furthermore, with regard to the citation of journal articles to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely the latest examples. Applicants readily agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Applicants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is not the standard for patentability under 35 U.S.C. § 101. Applicants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the

art would find any of the utilities described for the invention to be believable. Applicants submit that the overwhelming majority of those of skill in the relevant art would believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by hundreds if not thousands of journal articles, and would thus believe that Applicants sequence is a calcium channel protein. As believability is the standard for meeting the utility requirement of 35 U.S.C. § 101, and not 100% consensus or 100% accuracy, Applicants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

The Examiner states that "since the polypeptide encoded by the instant nucleic acid is not 100% identical to the AY029200 polynucleotide, the function of the polypeptide encoded by the instant nucleic acid is still not known' (Action at page 6). However, Applicants respectfully point out that the **PTO itself** does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials only requires a similarity score greater than 95% to establish functional homology. Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Applicants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as irrelevant to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

The Action additionally states that "(s)ince the AY029200 polynucleotide is a post-filing reference, the asserted utility was not well-established at the time of filing" (Action at page 6). Applicants respectfully point out that this argument is completely irrelevant to the utility issue at question here. Applicants point out that the utility of the presently claimed sequence as a calcium channel protein was clearly asserted in the specification as originally filed, which is all that is required under 35 U.S.C. § 101. That others later confirm Applicants asserted utility to be true does not mean that the utility as originally asserted does not meet the requirements of 35 U.S.C. § 101.

Finally, as set forth in the previous response, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well

aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in the previous response, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

III. Rejection of Claims 1 and 5-9 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, since

allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1 and 5-9 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Murphy have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

August 28, 2003
Date

David W. Hibler Reg. No. 41,071
Agent for Applicants

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399

Customer # 24231